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| 09/990,832 | 11/16/2001 | Andrew Howard Baker | 9013.22 | 3015 |

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MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

| EXAMINER | |
|---|---|
| KAM, CHIH MIN | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1653 | |

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/990,832 | BAKER ET AL. | |
| | Examiner | Art Unit | |
| | Chih-Min Kam | 1653 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**P riod for R ply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-3,5-10,12-18,28-30 and 32-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-10,12-18,28-30 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4/22/02* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: .

## DETAILED ACTION

### *Oath/Declaration*

1. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because non-dated alteration has been made to the name of the inventor, Stephen John White. See 37 CFR 1.52(c).

### *Election/Restrictions*

2. Applicant's election with traverse of Group I, claims 1-18, 28-34 and 38, and SIGYPLP (SEQ ID NO:51) as a targeting peptide, drug delivery vehicle as a material targeted to a cell, a biologically active drug as a pharmaceutical active agent and pharmaceutically active agents as a molecular group in the Response filed September 2, 2003 is acknowledged. The traversal is on the ground(s) that a search for Groups II-IV would overlap with a search of Group I, and all the claims of Groups I-IV can be searched in class 514 with many sharing the same subclass. This is not found persuasive because the traversal is not on the grounds that the inventions are not independent and distinct, rather, the traversal is on the grounds that there is no serious search burden. As such restriction is proper if two or more claimed inventions are either independent **or** distinct. See MPEP 803. Furthermore, coexamination of each of the additional groups and sequences would require search of classes and sequences unnecessary for the examination of the elected claims. For example, if Group III were included, it would require additional search of class 435, subclass 69.1, and if Group IV were included, it would require search of class 424, subclass 9.1. Therefore, coexamination of each of these inventions would require a serious additional burden of search. Furthermore, the restriction groups have acquired a separate status

in the art as a separate subject for inventive effect and require independent searches. The search for each of the invention is not coextensive particularly with regard to the literature search. A reference which would anticipate the invention of one group would not necessarily anticipate or make obvious any of the other group. Moreover, as to the question of burden of search, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not co-extensive and is much more important in evaluating the burden of search. Burden in examining materially different groups having materially different issues also exist. Claims 19-27, 35-37 and 39-43 of Groups II-IV and claims 4, 11, 31 and 38 of Group I are non-elected inventions, thus they are withdrawn from consideration. Therefore, claims 1-3, 5-10, 12-18, 28-30 and 32-34 are examined.

The requirement is still deemed proper and is therefore made FINAL.

***Informalities***

The disclosure is objected to because of the following informalities:

3. The specification recites amino acid and nucleotide sequences (e.g., pages 2, 3, 14, Table 5), however, the sequence identifier "SEQ ID NO:" is not indicated for the cited sequence. Applicant must comply with the requirements of sequence rules (37 CFR 1.821-1.825) and identify each sequence with a "SEQ ID NO:". Appropriate correction is required.

4. The specification recites polar amino acids are A, F, G, I, L, M, P, V, W, and non-polar amino acids are C, N, Q, S, T, Y at page 8, lines 27-28, which are not correct because A, F, G, I, L, M, P, V and W are non-polar residues, and C, N, Q, S, T and Y are polar residues (see Voet et al., Biochemistry, pages 60-61, 1990). Appropriate correction is required.

### *Claim Objections*

5. Claims 1-3, 7-10, 13, 28-30 and 34 are objected to because the claim contains recitation of non-elected inventions.

6. Claims 1-3, 8-10 and 28-30 are objected to because the claims recite amino acid sequences without indicating a "SEQ ID NO:" for the sequence.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3, 5-10, 12-18, 28-30 and 32-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a targeting peptide of SIGYPLP (SEQ ID NO:51) which targets gene delivery vectors such as adenoviral vectors to human endothelial cells (HEC), and a kit comprising the targeting peptide for use in transfecting HEC in vitro; or a peptide of SIGYPLP which targets adenoviral vectors to human vascular endothelial cells as indicated in the prior art, does not reasonably provide enablement for a targeting peptide of a SIGYPLP derivative for targeting a material to a cell; a pharmaceutical composition comprising a targeting peptide comprising SIGYPLP or a derivative thereof in association with a vehicle, wherein the vehicle carries a biologically active drug; and a kit comprising the targeting peptide of a SIGYPLP derivative for transfecting or identifying cell types in vitro, where the structure of SIGYPLP derivative, the targeted material and cell are not defined. The specification does not enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-3, 5-10, 12-18, 28-30 and 32-34 encompass a targeting peptide comprising SIGYPLP or a derivative thereof for targeting a material to a cell (claims 1-3 and 5-7); a pharmaceutical composition comprising a targeting peptide comprising SIGYPLP or a derivative thereof in association with a vehicle, wherein the vehicle carries a biologically active drug (claims 8-10 and 12-18); and a kit comprising a targeting peptide comprising SIGYPLP or a derivative thereof for transfecting or identifying cell types in vitro (claims 28-30 and 32-34). The specification, however, only discloses cursory conclusions without data supporting the findings, which state that the present invention provides a targeting peptide comprising a SIGYPLP or a derivative thereof for targeting a material to a cell, a pharmaceutical composition comprising a targeting peptide in association with a vehicle comprising a drug; and a kit comprising a targeting peptide for transfecting or identifying cell types in vitro (pages 2-3 and 9-11). There are no indicia that the present application enables the full scope in view of a targeting peptide comprising SIGYPLP or a derivative, or a pharmaceutical composition or a kit comprising the targeting peptide as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the

art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the derivatives of SIGYPLP as the targeting peptide, the pharmaceutical composition comprising SIGYPLP or its derivative and the drug, or the kit comprising the SIGYPLP derivative, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

Examples 1-4 demonstrates filamentous peptide phage display is used to isolate a panel of peptides that binds selectively and efficiently to human umbilical vein endothelial cells (HUVECs) with reduced binding to non-endothelial cells, and by biopanning on HUVECs, SIGYPLP is identified as a targeting peptide, which retargets gene delivery specifically to human vascular endothelial cells with a significantly enhanced efficiency over non-targeted adenovirus and without transduction of non-target cells. However, there are no working examples demonstrating a derivative of SIGYPLP as the targeting peptide, or a pharmaceutical composition comprising SIGYPLP or a derivative thereof and an identified drug.

(3). The state of the prior art and relative skill of those in the art:

The prior art (e.g., references cited at pages 7-8 of the specification) indicate the material to be targeted to cells includes drug-delivery or gene therapy vehicles such as liposomes, viruses or bacteria, and drug delivery vehicles may comprise a pharmaceutically active agent such as anti-tumor agents which are selectively targeted to tumor cells using the targeting peptides; Nicklin *et al.* (Circulation, 102, pages 231-237 (July 11, 2000)) teach filamentous peptide phage

display is used to pan primary human umbilical vein endothelial cells and to identify SIGYPLP as a targeting peptide which retargets gene delivery specifically to human vascular endothelial cells. However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide teachings on the identities of SIGYPLP derivatives and the effects of these peptides for targeting various biologically active drugs to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass a targeting peptide comprising SIGYPLP or a derivative thereof for targeting a material to a cell; a pharmaceutical composition comprising the targeting peptide; and a kit comprising a targeting peptide for transfecting or identifying cell types in vitro, however, the identities of SIGYPLP derivatives and the use of these peptides as targeting peptides are not adequately described in the specification, the invention is highly unpredictable regarding the effects of these targeting peptides in delivering the drugs to the target site.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a targeting peptide comprising SIGYPLP or a derivative thereof for targeting a material to a cell; a pharmaceutical composition comprising the targeting peptide; and a kit comprising a targeting peptide for transfecting or identifying cell types in vitro. The specification indicates filamentous peptide phage display is used to isolate a panel of peptides that binds selectively and efficiently to human umbilical vein endothelial cells (HUVECs) with reduced binding to non-endothelial cells, and by biopanning on HUVECs, SIGYPLP is identified as a targeting peptide, which retargets gene delivery specifically to human

vascular endothelial cells with a significantly enhanced efficiency over non-targeted adenovirus and without transduction of non-target cells (Examples 1-4). The specification further indicates the derivatives are the modified forms of the targeting peptides which retain the activity of the disclosed peptides, and derivatives may have amino acid substitutions in the form of like for like or like for non-like (page 8, line 7-page 9, line 4). However, the specification has not identified a specific SIGYPLP derivative used as a targeting peptide, nor has demonstrated the effect of SIGYPLP or a derivative thereof in a pharmaceutical composition to target a biologically active drug to a specific cell. Moreover, there are no working examples demonstrating a derivative of SIGYPLP is used as the targeting peptide, or a biologically active drug in the pharmaceutical composition is targeted by an identified peptide to a specific cell. Since the specification fails to provide sufficient teachings on identities of various SIGYPLP derivatives and the use of SIGYPLP or a derivative thereof in targeting a biologically active drug to a specific site, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of SIGYPLP or its derivatives in targeting various biologically active drugs to a specific cell.

(6). Nature of the Invention

The scope of the claims encompasses a targeting peptide comprising SIGYPLP or a derivative thereof for targeting a material to a cell, or a pharmaceutical composition or a kit comprising the targeting peptide, but the specification does not demonstrate the use of SIGYPLP or its derivatives in a pharmaceutical composition. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broader than the enabling disclosure. The working examples do not demonstrate the claimed variants, the effects of the derivatives are unpredictable, and the teachings in the specification are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the effects of SIGYPLP or its derivatives in targeting various biologically active drugs.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-3, 5-10, 12-18, 28-30 and 32-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 1-3, 5-10, 12-18, 28-30 and 32-34 are indefinite because of the use of the term "a derivative thereof". The term "a derivative thereof" renders the claim indefinite, it is not clear what structure the derivative has, and how different the derivative is from the parent compound. Claim 1 is also indefinite as to "a material", it is not clear what compound the material is. Claims 2-3, 5-7, 9, 10, 12-18, 29-30 and 32-34 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

10. Claims 28-30 and 32-34 are indefinite because of the use of the term "a kit comprising a targeting peptide". The term "a kit comprising a targeting peptide" renders the claim indefinite, it is not clear what else is included in the kit besides the targeting peptide. Claims 29-30 and 32-34 are included in this rejection for being dependent on a rejected claim and not correcting the deficiency of the claim from which they depend.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

11. Claims 1-3 and 5-6 are rejected under 35 U.S.C. 102(a) as being anticipated by White *et al.* (Abstract in 2nd Imperial College School of Medicine and Kennedy Institute of Rheumatology Symposium, November 22, 1999).

White *et al.* teach 7-mer peptide phage display libraries are used to pan primary human umbilical vein endothelial cells and to identify a peptide of SIGYPLP which targets adenoviral vectors to human vascular endothelial cells (abstract, claims 1-3 and 5-6).

12. Claims 1-3 and 5-6 are rejected under 35 U.S.C. 102(a) as being anticipated by Nicklin *et al.* (Circulation, 102, pages 231-237 (July 11, 2000)).

Nicklin *et al.* teach filamentous peptide phage display is used to isolate a panel of peptides that binds selectively and efficiently to human umbilical vein endothelial cells (HUVECs) with reduced binding to non-endothelial cells, and by biopanning on HUVECs, a peptide of SIGYPLP is identified to retarget gene delivery specifically to human vascular endothelial cells with a significantly enhanced efficiency over non-targeted adenovirus and without transduction of non-target cells (pages 233-235, claims 1-3 and 5-6).

***Conclusion***

13. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, Ph. D. can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

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October 29, 2003

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600